Docket No.: 1254-0229P
(PATENT)

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of:
Akio MATSUDA et al.

Application No.: 10/617,217 Confirmation No.: 6837

Filed: July 11, 2003 Art Unit: 1631

For: NF-κ B ACTIVATING GENE Examiner: M. L. Borin

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

I, Mr. Shuji Muramatsu, hereby declare as follows:

1. I am a Japanese citizen, residing at 17-13 Tadewara, Fuji-shi, Shizuoka 416-0931, Japan.

2. I obtained an undergraduate degree from the Department of Agricultural Chemistry of Nagoya University in 1988 and completed a Master's degree in the Graduate School of Agriculture of Nagoya University in 1990. I began employment at Asahi Chemical Industry, Co., Ltd. in 1990. I am presently employed at the Laboratory for Drug Discovery, Life Science Research Institute of Asahi Kasei Pharma Company. I have been engaged in research activity for approximately 20 years and I am well-versed in gene technology and molecular biology.

3. I am a co-inventor of the subject matter (or describe other relationship) of the above-identified U.S. Patent application. I am familiar with the specification and pending claims, and with the prosecution history of the application.

4. The Examiner has rejected claims 3-6 under 35 USC § 102(e) as lacking novelty over SEQ ID NO: 15 of the United States Patent Application Publication 20030012966 ("US '966"). The Examiner asserts that the reference sequence is 99% identical to the sequence shown in SEQ ID NO: 88 of the present application and therefore anticipates the invention claimed in the present application.

5. The alignment of SEQ ID NO: 15 of US '966 and SEQ ID NO: 88 of the present application attached as Figure A and used by the Examiner to make this assertion shows near identity from nucleotides 22 to 1860 of SEQ ID NO: 15 and 345 to 2183 of SEQ ID NO: 88. Thus, these two nucleotide sequences are distinct one from another at their 5' ends. There is also a nucleotide substitution; a C residue at position 974 in SEQ ID NO: 88 is shown as a T residue at position 651in SEQ ID NO: 15. Therefore, the recitation in claim 4 that the polynucleotide of the invention comprises the polynucleotide of SEQ ID NO: 88 is not met by the reference.

6. Despite the 99% identity at the nucleotide sequence level of SEQ ID NO: 15 of US '966 (hereinafter merely "SEQ ID NO: 15") and SEQ ID NO: 88 of the present application (hereinafter merely "SEQ ID NO: 88") asserted by the Examiner, there are functional differences between these sequences that distinguish the presently claimed invention from the disclosure of US '966. In particular, proteins encoded by SEQ ID NO: 15 of US '966 do not exhibit any activity as activators of NF-kB, while the protein encoded by SEQ ID NO: 88 (i.e. the protein having the amino acid sequence of SEQ ID NO: 87) is an activator of NF-kB transcription factor activity.

7. To demonstrate this result, the experiments described hereinbelow were performed by me or under my supervision.

8. As a threshold matter, it should be noted that the amino terminal amino acid sequence of SEQ ID NO: 87 includes the amino acid sequence Met-Gly-Ile-Gly-Lys. Inspection of SEQ ID NO: 34 and SEQ ID NO: 53 shows that neither of these sequences include this amino acid sequence. Therefore, the recitation of claim 3 that the nucleotide sequence encodes the amino acid sequence of SEQ ID NO: 87 is not met by SEQ ID NO: 15.

9. Second, it should be noted that the 5' end of the polynucleotide sequence of SEQ ID NO: 15 does not include any translation initiation codon corresponding to SEQ ID NO: 53 of US '966. (hereinafter merely "SEQ ID NO: 53"). That is, one should consider that SEQ ID NO: 53 begins with an isoleucine residue rather than a methionine. SEQ ID NO: 34 of US '966 (hereinafter merely "SEQ ID NO: 34") is also encoded by SEQ ID NO: 15 and does begin with a methionine residue. Therefore, both of the polypeptides of SEQ ID NO: 34 and SEQ ID NO: 53 were expressed as fusion proteins with a Green Fluorescence Protein as shown in the attached Figure B.

10. In this regard, the polynucleotide encoding SEQ ID NO: 15 was prepared by fusing the 3' end of the GFP-encoding sequence to the polynucleotide encoding SEQ ID NO: 34 at the amino-terminal methionine in the vector pcDNA3.1. Similarly, the 3' end of the GFP-encoding sequence was fused to the nucleotide sequence encoding SEQ ID NO: 53 at the amino-terminal isoleucine residue. Finally, a similar vector was prepared fusing the 3' end of the GFP-encoding sequence to the nucleotide sequence encoding SEQ ID NO: 87 at the amino-terminal isoleucine residue.

11. The expression vectors encoding the GFP fusion proteins were co-transfected into cultured 293EBNA cells with a luciferase expression vector in which transcription of a luciferase-encoding polynucleotide is controlled by NF-kB activity, and luciferase expression was measured in the

same manner as the reporter assay described in Example 2 beginning at page 64 of the present specification. 10, 25, 50 or 100 ng/well of the GFP fusion vectors were co-transfected with 50 ng of the NF-kB:luciferase expression vector.

12. The results of the reporter assays are shown in the attached Figure C. These results clearly demonstrate that the protein of SEQ ID NO: 87 encoded by the nucleotide sequence of SEQ ID NO: 88 of the present application has activity of activating NF-kB. On the other hand, the two polypeptides of SEQ ID NO: 34 and 53, encoded by the nucleotide sequence of SEQ ID NO: 15 of the reference, do not have NF-kB activating activity.

13. To confirm that the negative result obtained using the vectors expressing GFP-SEQ ID NO:34 and GFP-SEQ ID NO:53 fusions was not due to lack of expression of the fusion protein, an aliquot of the proteins from cells used in the reporter assay was evaluated by Western blotting using anti-GFP antibody. The results of the Western blot are shown in Figure D, and it is plainly seen that similar amounts of protein were expressed by each GFP fusion protein expression vector. Therefore, the lack of NF-kB activation by GFP-SEQ ID NO:34 and by GFP-SEQ ID NO:53 was not due to a lack of expression of the fusion protein.

14. The results of the luciferase reporter assay establish that SEQ ID NO:15 does not encode any protein that activates NF-kB. Therefore, the recitation of claims 3-6 that the protein encoded by the polypeptide "activates NF-kB" is also not met.

15. None of the recitations in claims 3-6 are completely met by the polynucleotide of SEQ ID NO: 15 of US '966 or the proteins it encodes. Therefore, this reference does not describe any polynucleotide within the scope of claims 3-6 and therefore the invention described by the present

claims 3-6 is neither disclosed nor suggested to one of ordinary skill in the art who reads this reference.

16. Should the invention of claims 3-6 be deemed obvious at first glance over SEQ ID NO: 15, in view of the Examiner's premise that nearly identical nucleotide sequences must encode proteins having the same activity the finding that SEQ ID NO: 83 of the instant application encodes a protein having NF-kB activation activity, but SEQ ID NO: 15 does not, must be taken as a result that is unexpected by one of ordinary skill in the art reading US '966. 17. I hereby declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

Date: June. 20. 2006 By Shuji Muramatsu
Mr. Shuji Muramatsu

Figure A

RESULT 5
US-09-768-826-15
; Sequence 15, Application US/09768826
; Patent No. US20020012966A1
; GENERAL INFORMATION:
; APPLICANT: Shi et al.
; TITLE OF INVENTION: 18 human secreted proteins
; FILE REFERENCE: PP512P1
; CURRENT APPLICATION NUMBER: US/09/768,826
; CURRENT FILING DATE: 2001-01-25

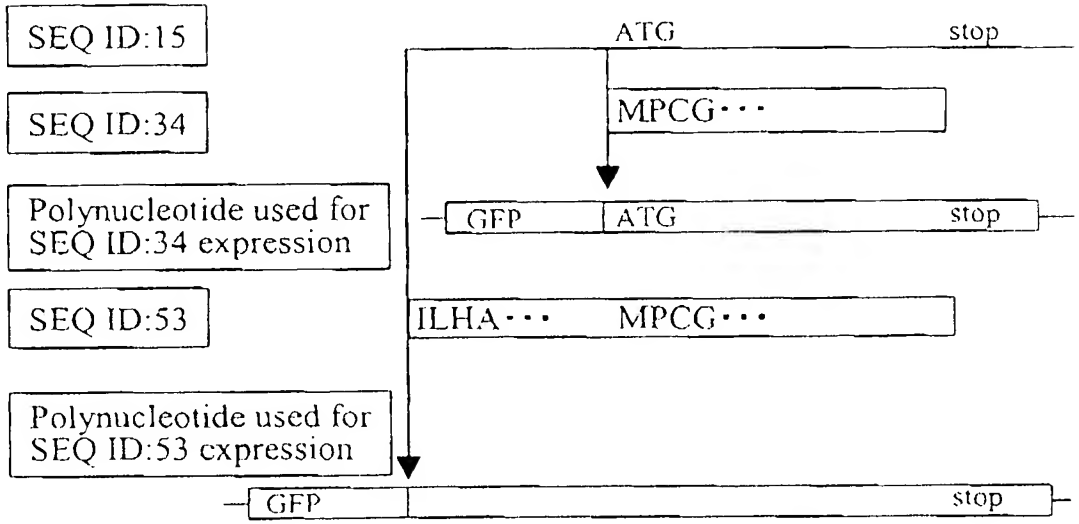

Figure B

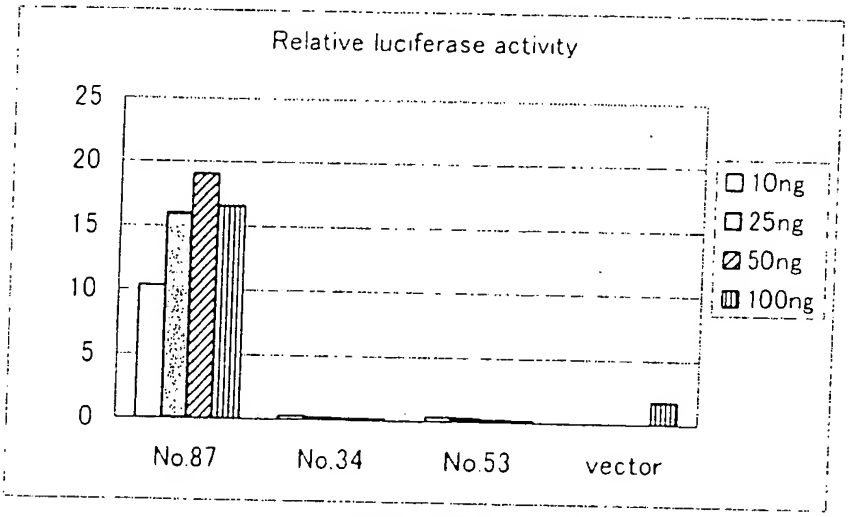

Figure C

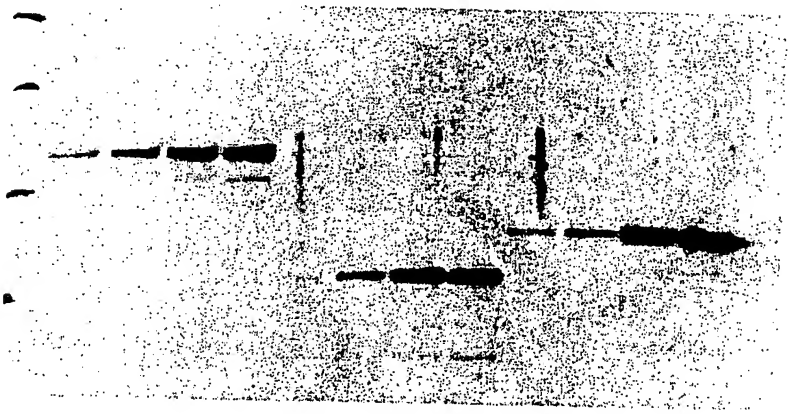

Figure D

No.87 No.34 No.53

PRIOR APPLICATION NUMBER: PCT/US00/22350
PRIOR FILING DATE: 2000-08-15
PRIOR APPLICATION NUMBER: 60/148,759
PRIOR FILING DATE: 1999-08-16
NUMBER OF SEQ ID NOS: 61
SOFTWARE: PatentIn Ver. 2.0
SEQ ID NO 15
LENGTH: 1860
TYPE: DNA
ORGANISM Homo sapiens
US-09-768-826-15

Query Match 67.6%; Score 1635.8; DB 9; Length 1860,
Best Local Similarity 99.9%; Pred. No. 0;
Matches 1837, Conservative 0; Mismatches 2; Indels 0, Gaps 0;

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Qy        345 CTCAAATTTGTGATATTGCATGCAGAAGATGACACAGATGAAGCCCTCAGAGTCCAGAAT 404
Db         22 CTCAAATTTGTGATATTGCATGCAGAAGATGACACAGATGAAGCCCTCAGAGTCCAGAAT 81
Qy        405 CTGCTACAAGATGACTTTGGTATCAAACCCGGAATAATCTTTGCTGAGATGCCATGTGGC 464
Db         82 CTGCTACAAGATGACTTTGGTATCAAACCCGGAATAATCTTTGCTGAGATGCCATGTGGC 141
Qy        465 AGACAGCATTTACAGAATTTAGATGATGCTGTAAATGGGTCTGCATGGACAATCTTATTA 524
Db        142 AGACAGCATTTACAGAATTTAGATGATGCTGTAAATGGGTCTGCATGGACAATCTTATTA 201
Qy        525 CTGACTGAAAACTTTTTAAGAGATACTTGGTGTAATTTCCAGTTCTATACGTCCCTAATG 584
Db        202 CTGACTGAAAACTTTTTAAGAGATACTTGGTGTAATTTCCAGTTCTATACGTCCCTAATG 261
Qy        585 AACTCCGTTAACAGGCAGCATAAATACAACTCTGTTATACCCATGCGGCCCCCTGAACAAT 644
Db        262 AACTCCGTTAACAGGCAGCATAAATACAACTCTGTTATACCCATGCGGCCCCCTGAACAAT 321
Qy        645 CCCCTTCCCCCGAGAAAGGACTCCCTTTGCCCTCCAAACCATCAATGCCTTAGAGGAAGAA 704
Db        322 CCCCTTCCCCCGAGAAAGGACTCCCTTTGCCCTCCAAACCATCAATGCCTTAGAGGAAGAA 381
Qy        705 AGTCGTGGATTTCCTACACAAGTAGAAAGAATTTTTCAGGAGTCTGTGTATAAGACACAA 764
Db        382 AGTCGTGGATTTCCTACACAAGTAGAAAGAATTTTTCAGGAGTCTGTGTATAAGACACAA 441
Qy        765 CAAACTATATGGAAAGAGACAAGAAATATGGTACAAAGACAATTTATTGCCTGAGATGAA 824
Db        442 CAAACTATATGGAAAGAGACAAGAAATATGGTACAAAGACAATTTATTGCCTGAGATGAA 501
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Db        502 ACATATAACATGTGGCTGGCTCTTGTTTTGTAAACCAAATGATTAATCTTCACTTGAGAA 561
Qy        885 AGCAGTTTCTAGGAAATGTTTAAATAAAAGAGAGTCTTCACCTTAAAGAAACCTATGGAG 944
Db        562 AGCAGTTTCTAGGAAATGTTTAAATAAAAGAGAGTCTTCACCTTAAAGAAACCTATGGAG 621
Qy        945 CACAAGAAAGATAAATTTCTGCAGGACAGCCTATAAAATTGTGGTACTTTTTGATGTTTC 1004
Db        622 CACAAGAAAGATAAATTTCTGCAGGACAGTCTATAAAATTGTGGTACTTTTTGATGTTTC 681
Qy       1005 AGTAAACTTGACATTGTCAGAGTTTCAAGGACTTTTCTTTCACAATTTTCCTAGTTCATG 1064
Db        682 AGTAAACTTGACATTGTCAGAGTTTCAAGGACTTTTCTTTCACAATTTTCCTAGTTCATG 741
Qy       1065 GATATGAAAAAGGAATTCTCAATCCATATTCCTTGTATTGAACCTTGAACAAAAACTTGT 1124
Db        742 GATATGAAAAAGGAATTCTCAATCCATATTCCTTGTATTGAACCTTGAACAAAAACTTGT 801
Qy       1125 ATGACAGACATTTTTAAAAATGTGACAACACTTTTATTCTCTGAATTTTGATCTCAAAGG 1184
Db        802 ATGACAGACATTTTTAAAAATGTGACAACACTTTTATTCTCTGAATTTTGATCTCAAAGG 861
Qy       1185 ACACAGAAAAAAAAATGGCCCCAGGAGATCTGATCACACTTCCTCCTGAGGCACCTCTCAT 1244
Db        862 ACACAGAAAAAAAAATGGCCCCAGGAGATCTGATCACACTTCCTCCTGAGGCACCTCTCAT 921
Qy       1245 GGATGTTGCAATAAGCATTCGGGTACTATCACCCAGAAATATGAATTGCCAGAATAGAAC 1304
Db        922 GGATGTTGCAATAAGCATTCGGGTACTATCACCCAGAAATATGAATTGCCAGAATAGAAC 981
Qy       1305 ATTTAGCATGTTAAGCGTTGATGCATATAAAATCAGAAATAGATGTGAGAATGGTGGAAC 1364
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Qy       1365 TTTTTAAAAGAACCCAGTCAAATGTATTTTCTGCTGAAATCTGCATATTTGGAGGCATTT 1424
Db        1042 TTTTTAAAAGAACCCAGTCAAATGTATTTTCTGCTGAAATCTGCATATTTGGAGGCATTT 1101
Qy       1425 CCCACCACCGATTCACAGCCCATTTGATAGTGTGGTAGTTAGGGACTTCGTGGAGTGGTG 1484
Db        1102 CCCACCACCGATTCACAGCCCATTTGATAGTGTGGTAGTTAGGGACTTCGTGGAGTGGTG 1161
Qy       1485 TTCAGACGTCCCCTGGGGCTTAAATCTCTTCATATTAGTCATCATTTGTAACTATGGCTT 1544
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Qy       1545 TATTTGCAGAGCTTCTAAAAGGCGTATAACTGTGTGAGTGGCCAGATATTCACTTTTTAG 1604
Db        1222 TATTTGCAGAGCTTCTAAAAGGCGTATAACTGTGTGAGTGGCCAGATATTCACTTTTTAG 1281
Qy       1605 ATCAAAAACCTCTCTTATGGAAGCTTTAAAAGTTTCCGTCACACACAATTCTCTTCTCAG 1664
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Qy       1725 GGTTATTTATAAAGACTTTGGATAGAAGGAGATGTATTTTATTACCTCCTATTCTAGAGC 1784
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Qy       1785 CCCATGCTCCTAACAAGCCAGAGAGGCCCCAAACAGGATTGTTTCTTTCCTCCACAGCCC 1844
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Qy       1905 TGGGTCATGTCATGTAATGAGAAAAGCCCTCTTCGGGATCATGAGACTTGGTTCTAGTCC 1964
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RESULT 6
US-10-874-484-15
; Sequence 15, Application US/10874484
; Publication No. US20040235113A1
; GENERAL INFORMATION: